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·临床研究·

CK-MB、MYO、hs-cTnT对脓毒症患者心肌损伤的诊断意义

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[摘 要] **目的** 探讨血清肌酸激酶同工酶MB(CK-MB)、肌红蛋白(MYO)、高敏肌钙蛋白T(hs-cTnT)检测对脓毒症患者心肌损伤的诊断价值。**方法** 选取我院收治的132例脓毒症患者,根据患者是否存在心肌损伤分为心肌损伤组(50例)和非心肌损伤组(82例),根据脓毒症患者心肌损伤严重程度分为轻度组(33例)和重度组(17例)。采用电化学发光法检测患者血清CK-MB、MYO、hs-cTnT水平;采用受试者工作特征(*ROC*)曲线分析血清CK-MB、MYO、hs-cTnT水平对脓毒症患者心肌损伤的诊断价值,计算灵敏度、特异度、曲线下面积(*AUC*)。**结果** 心肌损伤组患者血清CK-MB、MYO、hs-cTnT水平均高于非心肌损伤组($P<0.05$)。重度组患者血清CK-MB、MYO、hs-cTnT水平均高于轻度组($P<0.05$)。*ROC曲线*结果显示,血清CK-MB、MYO、hs-cTnT联合检测诊断脓毒症患者心肌损伤的灵敏度和*AUC*均高于单独检测($P<0.05$)。**结论** 脓毒症心肌损伤患者血清CK-MB、MYO、hs-cTnT水平升高,且心肌重度损伤患者以上指标水平均高于轻度损伤患者,检测血清CK-MB、MYO、hs-cTnT均对脓毒症患者心肌损伤有一定的诊断价值,而三者联合检测诊断价值更高。

[关键词] 肌酸激酶同工酶MB;肌红蛋白;高敏肌钙蛋白T;脓毒症;心肌损伤

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Diagnostic significance of CK-MB, MYO and hs-cTnT for myocardial injury in patients with sepsis

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Abstract: Objective To investigate the diagnostic values of serum creatine kinase-MB (CK-MB), myoglobin (MYO) and hypersensitive cardiac troponin T (hs-cTnT) detection for myocardial injury in patients with sepsis. **Methods** A total of 132 patients with sepsis admitted to our hospital were selected, and they were divided into the myocardial injury group (50 cases) and non-myocardial injury group (82 cases) according to whether the patients had myocardial injury, and sepsis patients with myocardial injury were divided into the mild group (33 cases)

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and severe group (17 cases) according to their severity. The levels of serum CK-MB, MYO and hs-cTnT of patients were detected by electrochemiluminescence assay. The diagnostic values of serum CK-MB, MYO and hs-cTnT levels on myocardial injury in patients with sepsis were analyzed by the *receiver operating characteristic* (*ROC*) curve, and the sensitivity, specificity and *area under the curve* (*AUC*) were calculated. **Results** The levels of serum CK-MB, MYO and hs-cTnT in the myocardial injury group were higher than those in the non-myocardial injury group ($P<0.05$). The levels of serum CK-MB, MYO and hs-cTnT in the severe group were higher than those in the mild group ($P<0.05$). *ROC* curve results showed that the sensitivity and *AUC* of combined detection of serum CK-MB, MYO and hs-cTnT to diagnose myocardial injury in patients with sepsis were higher than those of individual detection ($P<0.05$). **Conclusion** The levels of serum CK-MB, MYO and hs-cTnT are increased in sepsis patients with myocardial injury, and the levels of the above indicators in patients with severe myocardial injury were higher than those in patients with mild myocardial injury. The detections of serum CK-MB, MYO and hs-cTnT have certain diagnostic value for myocardial injury in patients with sepsis, and the diagnostic value of the combined detection is higher.

Keywords: creatine kinase-MB; myoglobin; hypersensitive cardiac troponin T; sepsis; myocardial injury

脓毒症是由多种感染、创伤导致的器官功能障碍综合病症，患者常表现为心慌、寒战、精神状态改变等。该病发病机制复杂，且病情凶险，严重时可造成多器官功能障碍，病死率较高[1]。心肌损伤是脓毒症常见并发症之一，可影响患者心脏功能，增加死亡风险[2]。研究显示，脓毒症患者并发心肌损伤的发生率高达40%左右，而伴有心肌损伤的患者病死率远高于无心肌损伤的患者[3]。因此，临床需要寻找合适的指标准确评估脓毒症患者的心肌损伤，进而指导临床治疗。目前常通过检测血清肌酸激酶同工酶MB（creatine kinase-MB, CK-MB）、肌红蛋白（myoglobin, MYO）及肌钙蛋白等心肌损伤标志物对心肌损伤进行临床评估和病情监测[4]。既往研究报道，肌钙蛋白T（cardiac troponin T, cTnT）、CK-MB、MYO均对急性心肌梗死有一定诊断价值，可为临床早期病情诊断提供依据[5]。鉴于血清高敏肌钙蛋白T（hypersensitive cardiac troponin T,hs-cTnT）较cTnT灵敏度更高[6]，故本研究联合检测血清hs-cTnT、CK-MB、MYO用于脓毒症患者心肌损伤的诊断，并分析以上指标与心肌损伤的相关性，现报告如下。

1 资料与方法

1.1 临床资料

选取我院2019年11月至2021年11月收治的脓毒症患者132例，其中男73例，女59例；年龄46~78岁，平均（65.84±10.12）岁；BMI为（23.25±2.16）kg/m^2；感染部位：肺部57例，腹腔31例，泌尿系统22例，皮肤软组织14例，其他8例。脓毒症诊断参照《中国脓毒症/脓毒性休克急诊治疗指南》（2018）[7]中相关诊断标准：体温高于38.3 ℃或低于36.0 ℃，心率超过90次/分或超过同龄人正常值的2个标准差，收缩压低于90 mmHg；精神状态不佳，严重时有休克表现；血浆C反应蛋白、降钙素原水平升高，白细胞计数大于12×10^9/L；血液中乳酸水平大于1 mmol/L，毛细血管再灌注能力下降，皮肤表面有瘀斑形成等。纳入标准：符合脓毒症的诊断标准；年龄在18岁以上。排除标准：处于妊娠期、哺乳期；合并血液性系统疾病或恶性肿瘤；精神障碍；伴有急性心梗、心脏病等心脏器质性病变；有心脏手术史；近期接受过激素、免疫抑制药物治疗；资料不全；肝、肾等重要器官功能不全。本研究经我院伦理委员会审批（201910-004），患者均对本研究知情同意。

1.2 方法

患者于入院24 h内采集外周静脉血5 mL，离心分离出血清，使用全自动生化分析仪按照电化学发光法检测血清CK-MB、MYO、hs-cTnT水平。血清CK-MB正常参考范围：0~18 U/L；血清MYO正常参考范围：10~85 μg/L；血清hs-cTnT正常参考范围：0~40 ng/L。

脓毒症心肌损伤判定标准[8]：①心电图异常改变，ST段异常抬高或有异常Q波；②影像学检查结果显示心脏结构、功能改变或异常，左心室射血分数<50%；③cTnT≥0.15 ng/mL。根据是否存在心肌损伤将患者分为心肌损伤组（50例）和非心肌损伤组（82例），比较2组患者CK-MB、MYO、hs-cTnT水平。

心肌损伤严重程度分级[9]：cTnT升高水平低于5倍参考值上限为轻度；cTnT升高水平在5倍参考值上限及以上为重度。依据此标准将脓毒症心肌损伤患者分为轻度组（33例）和重度组（17例），比较2组患者CK-MB、MYO、hs-cTnT水平。

1.3 统计学分析

以SPSS 26.0软件行统计学分析，计量资料经正态检验，不符合正态分布的数据以中位数（四分位间距）[*M*(*Q*1, *Q*3)]表示，行*Mann-Whitney U*检验；计数资料以率（%）表示，行χ^2检验。采用受试者工作特征（*receiver operating characteristic*, *ROC*）曲线分析血清CK-MB、MYO、hs-cTnT联合检测对脓毒症患者心肌损伤的诊断价值，记录灵敏度、特异度、曲线下面积（*area under the curve*, *AUC*）及其95%*CI*。

2 结果

2.1 心肌损伤组和非心肌损伤组患者血清CK-MB、MYO、hs-cTnT水平比较

心肌损伤组血清CK-MB、MYO、hs-cTnT水平均高于非心肌损伤组(P<0.05),见表1。

2.2 轻度组和重度组患者血清CK-MB、MYO、hs-cTnT水平比较

重度组血清CK-MB、MYO、hs-cTnT水平均高于轻度组(P<0.05),见表2。

表1 心肌损伤组和非心肌损伤组血清CK-MB、MYO、hs-cTnT水平[M($Q1$,$Q3$)]

组别	n	CK-MB(U/L)	MYO(μg/L)	hs-cTnT(ng/L)
心肌损伤组	50	30.24(16.53,30.63)	64.79(54.19,74.42)	45.52(27.98,69.20)
非心肌损伤组	82	13.65(13.27,14.74)	44.32(40.56,50.66)	22.32(20.55,26.09)
U		30.160	47.112	32.596
P		<0.001	<0.001	<0.001

表2 轻度组和重度组血清CK-MB、MYO、hs-cTnT水平[M($Q1$,$Q3$)]

组别	n	CK-MB(U/L)	MYO(μg/L)	hs-cTnT(ng/L)
轻度组	33	28.68(15.41,28.82)	62.92(51.46,70.09)	43.88(24.02,63.29)
重度组	17	33.26(18.25,33.78)	67.42(57.60,76.45)	48.71(31.25,72.60)
U		6.448	7.256	5.596
P		<0.001	<0.001	0.002

2.3 血清CK-MB、MYO、hs-cTnT单独及联合检测对脓毒症患者心肌损伤的诊断价值

血清CK-MB、MYO、hs-cTnT联合检测诊断脓毒症患者心肌损伤的灵敏度均高于单独诊断(χ^2=4.000,P=0.046;χ^2=6.061,P=0.014;χ^2=10.714,P=0.001),AUC均高于单独检测(Z=2.031,P=0.042;Z=2.524,P=0.012;Z=2.022,P=0.043),其特异度与单独检测比较差异无统计学意义(P>0.05),见表3、图1。

表3 血清CK-MB、MYO、hs-cTnT单独及联合检测对脓毒症患者心肌损伤的诊断价值

指标	Cut-off值	灵敏度(%)	特异度(%)	AUC	95%CI
CK-MB	28.36 U/L	84.00	82.93	0.787	0.707~0.853
MYO	53.42 μg/L	80.00	84.15	0.749	0.666~0.820
hs-cTnT	50.65 ng/L	72.00	91.46	0.797	0.718~0.862
联合检测		96.00	81.71	0.904	0.841~0.949

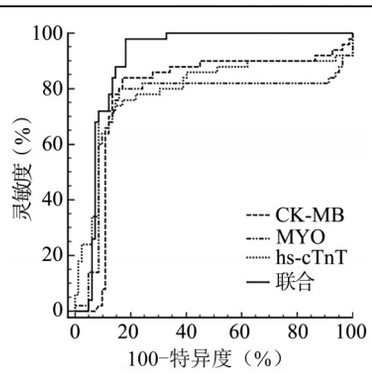


图1 血清CK-MB、MYO、hs-cTnT检测对脓毒症患者心肌损伤的诊断*ROC*曲线

3 讨论

脓毒症是由细菌等病原微生物侵入机体后引起的全身炎症反应,涉及多个器官,随着病情的进展可引起器官功能障碍及组织灌注不足,严重影响患者的健康[10]。脓毒症患者并发心肌损伤可加重疾病进展,增加死亡风险。因此,对脓毒症患者心肌损伤情况进行评估,并采取及时有效的干预措施对改善预后意义重大。

本研究结果发现,心肌损伤组患者血清CK-MB、MYO、hs-cTnT水平均高于非心肌损伤组,且心肌损伤患者重度组以上指标均高于轻度组,说明血清CK-MB、MYO、hs-cTnT水平在心肌损伤后升高,且其水平升高可能与心肌损伤严重程度有关。脓毒症患者心脏收缩能力下降,泵血能力降低,左心房压力升高,肺静脉回流阻力增大,易诱发心肌损伤。从发病机制上分析,脓毒症患者并发心肌损伤后,机体内毒素、自由基释放增多,细胞膜通透性增加,肌钙蛋白部分裂解产物进入外周循环,加重炎症反应。因此,脓毒症不仅可引起患者心脏组织损伤,对全身血流动力学都有一定影响,且心肌受损程度与患者的预后密切相关[11]。近年来,心肌损伤标志物的检测在临床中应用越来越广泛,可为病情诊断提供重要依据。CK-MB广泛存在于心肌的外浆层,是心脏中肌酸激酶的一种特殊成分,正常人血液中检测不到或只有微量存在;当心肌损伤后,心肌细胞破裂,释放肌酸激酶到血液中,CK-MB水平升高,且其升高水平与损伤程度成正比,检测其水平变化有助于判断患者心肌损伤的发生及病情进展程度[12]。唐晓芳等[13]研究报道,CK-MB在轮状病毒肠炎并发心肌损伤患者中水平升高,对心肌损伤有一定的诊断价值,本研究结果与之相符,说明CK-MB对脓毒症患者心肌损伤具有一定评估价值。MYO是一种小分子色素蛋白,在心肌细胞中有储存、转运氧的功能,心肌受损时即从心肌细胞中弥散进入

血液循环,在心肌梗死后0.5~2 h即可检测到其水平明显升高[14]。Asl等[15]研究中指出,MYO是心肌损伤后最早进入血液的指标,可能是检测心脏损伤的生物标志物。Pilut等[16]研究也发现,MYO、肌钙蛋白等水平在评估入住ICU和急性心脏事件方面有一定价值,定期评估这些生物标志物有助于对因COVID-19住院的心力衰竭患者进行疾病诊断和风险分层。hs-cTnT是原肌球蛋白结合亚基,是推动肌肉收缩的一种蛋白,仅存在于心肌中,具有良好的心肌特异性。Cheung等[17]研究发现,在儿童白血病患者诱导治疗阶段完成蒽环类药物治疗后,血浆hs-cTnT、循环miR-1水平显著升高,其中hs-cTnT水平与心肌的变化有关,可作为白血病儿童化疗期间心肌损伤的重要标志物,对评估患儿预后有一定指导意义,本研究结果与之基本一致,进一步说明hs-cTnT可用于脓毒症患者心肌损伤的诊断,并与患者心肌损伤程度相关。当心肌细胞损伤时,MYO是最早进入血液的生物标志物,扩散入血的速度比CK-MB、hs-cTnT快,但MYO在骨骼肌中也有表达,当骨骼肌损伤时也会出现其水平升高的情况,不具有心肌损伤特异性[18]。但hs-cTnT特异度高,心肌细胞损伤时,hs-cTnT进入血液的时间窗较长,不利于6 h内心肌损伤的诊断。鉴于这3个指标特异度和灵敏度不同,本研究将以上三者联合检测,结果显示三者联合诊断的灵敏度和*AUC*均高于单独诊断,在不降低特异度的情况下提高了诊断灵敏度,显著提高了脓毒症患者心肌损伤的临床诊断价值。

综上所述,血清CK-MB、MYO、hs-cTnT水平均是诊断脓毒症患者心肌损伤的有效指标,且三者联合检测对诊断心肌损伤的价值更高。但本研究样本量较小,血清CK-MB、MYO、hs-cTnT在脓毒症心肌损伤中的临床应用有待进一步研究。

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